CLINICAL AND EPIDEMIOLOGICAL STUDY OF BRONCHIAL ASTHMA IN CHILDREN & ASSESSMENT OF SEVERITY OF ASTHMA AND ITS CORRELATION WITH SERUM IgE LEVELS

Dissertation submitted to

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

In fulfillment of the regulations
for the award of
M.D DEGEREE IN PEDIATRIC MEDICINE

BRANCH VII

GOVERNMENT MOHAN KUMARAMAMGALAM

MEDICAL COLLEGE, SALEM

APRIL 2013

CERTIFICATE

Certified that this dissertation entitled **"CLINICAL AND EPIDEMIOLOGICAL STUDY OF BRONCHIAL ASTHMA IN CHILDREN & ASSESSMENT OF SEVERITY OF ASTHMA AND ITS CORRELATION WITH SERUM IgE LEVELS"** is a bonafide work done by **Dr.P.PRIYADHARSHINI** postgraduate student of Paediatric Medicine,Government Mohan Kumaramangalm Medical College, Salem-636030,during the Academic year 2010-2012.

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DECLARATION

I Solemnly declare that this dissertation "**CLINICAL AND EPIDEMIOLOGICAL STUDY OF BRONCHIAL ASTHMA IN CHILDREN & ASSESSMENT OF SEVERITY OF ASTHMA AND ITS CORRELATION WITH SERUM IgE LEVELS"** prepared by me at Government Mohan Kumaramangalam Medical College and Hospital,Salem-636030 under the guidance and supervision of **Prof.Dr.T.S.SUNDARARAJAN.M.D.,D.C.H.,** HOD of Pediatric Medicine and **Associate professor DR.D.SAMPATH KUMAR, M.D., D.C.H.,**Government Mohan Kumaramangalam Medical College and Hospital, Salem.

This Dissertation is submitted to **THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY, CHENNAI No table of contents entries found.**in partial fulfillment of the University regulation for the award of degree **M.D Branch VII (Pediatrics)** for April 2013

Place: Salem

Date: **DR.P.PRIYADHARSHINI**

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ABBREVATIONS

AHR ---------- Allergic Hyperresponsiveness

ecNOS ---------- Endothelial cell Nitric Oxide Synthetase

FEF ---------- Forced Expiratory Flow

FeNO ---------- Fractional Exhaled Nitric Oxide

FEV ---------- Forced Expiratory Volume

FVC ---------- Forced Vital Capacity

ICS ---------- Inhalational Corticosteroids

IgE ---------- Immunoglobulin E

iNOS ---------- Inducible Nitric Oxide Synthetase

LABs ---------- Long Acting inhaled Beta agonists

LTRAs ---------- Leukotriene Receptor Antagonists

NIH ---------- National Institute of Health

nNOS ---------- Neuronal Nitric Oxide Synthetase

NO ---------- Nitric Oxide

NOS ---------- Nitric Oxide Synthetase

NSAIDs ---------- Non Steroidal Anti Inflammatory Drugs

PC ---------- Provocative Concentration

PEFR ---------- Peak Expiratory Flow Rate

RSV ---------- Respiratory Syntitial Virus

SABAs ---------- Short Acting Inhaled Beta Agonist

TNF ----------Tumor Necrosis Factor

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ABSTRACT

BACKGROUND:

Bronchial asthma is a common chronic disease which is increasing in prevalence among children worldwide. IgE plays a major role in the pathogenesis of asthma. This study was done to assess the correlation of serum IgE levels with various grades of asthma and also the association of various epidemiological factors to the severity of asthma.

METHODOLOGY:

This is a case study performed over 75 asthmatic children who were attending outpatient as well those admitted in our pediatric ward from October 2011 to September 2012. The study also included 75 healthy controls. Detailed history including passive smoking, duration of breast feeding, family history and age of onset was taken. Severity of Asthma

was assessed clinically and by Spirometry. Serum IgE levels were estimated using Elisa kit.

RESULTS:

In our study there was significant association of serum IgE levels with the severity of asthma ($p < 0.005$). IgE levels did not differ significantly in different age groups and both sexes. Significant association was present between the severity of asthma and family history, passive smoking, atopic eczema, duration of breast feeding & duration of the disease ($p < 0.005$).

CONCLUSION:

IgE plays a definite role in the prevalence and severity of asthma. Estimation of serum IgE levels and assessment of severity helps in effective management of asthmatic children. Anti – IgE therapy will be beneficial in moderate to severe asthmatics. Promotion of breast feeding, avoidance of exposure to passive smoking and other triggering factors could reduce the severity of asthma thereby decreasing the morbidity and mortality.

KEYWORDS:

Bronchial asthma, IgE, Breast feeding, passive smoking and atopic eczema.

INTRODUCTION

Allergic respiratory diseases, particularly Bronchial asthma is increasing in prevalence among children globally. Asthma is the most common chronic disease worldwide. It affects persons of all ages.

Genetic predisposition is one of the reasons for increased prevalence in children and other factors like air pollution, urbanization and environmental tobacco smoke also contribute more significantly.

Asthma poses a significant burden not only in terms of health care costs but also of lost productivity and reduced participation in family life. When uncontrolled, Asthma place severe limits on daily life and is sometimes fatal.

DEFINITION OF BRONCHIAL ASTHMA:

Asthma is defined as a reversible chronic inflammatory condition of lung airways resulting in episodic air flow obstruction.It is characterized by recurrent episodes of wheezing, chest tightness and coughing alternating with periods of relatively normal breathing.

EPIDEMIOLOGY AND BURDEN OF ASTHMA:

The word asthma is derived from Greek verb “aazein” meaning to breathe hard. Asthma affects about 300 million people in the world.[1,2]

Various epidemiological studies carried out in different countries indicate the prevalence of respiratory allergic diseases as 14-30 percent. In children and adult the global prevalence of asthma ranges from 3.5-20% of the population in any country.[3]

The increase in prevalence over the last 25 years possibly reflects the changes in our environment (or) life style, greater awareness of this condition and improvements in diagnostic practices.

World wide, asthma cases are increasing at a rate of 50 percent every decade. The prevalence of asthma is the highest in developed

countries such as United States, United Kingdom, Australia, Newzealand and North West Europe and is increasing in developing countries like India.

The prevalence of asthma is higher in urban areas compared to rural areas. Most of the asthmatics develop symptoms before the age of ten. Among young children the prevalence of asthma is slightly higher in boys than in girls, however after puberty it is more common in female.

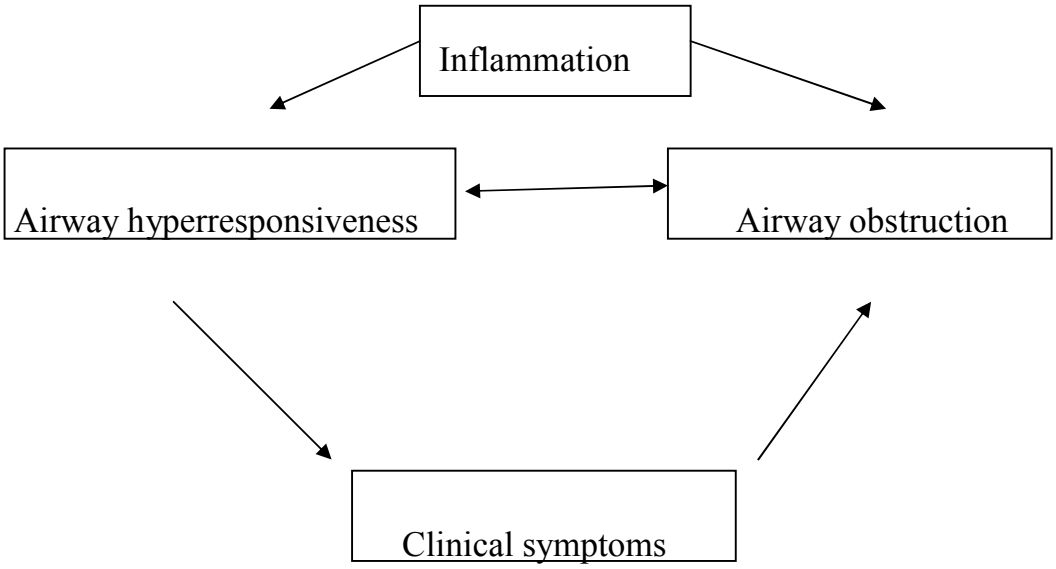
It has been estimated that our country has approximately 15-20 million asthmatics and it accounts for one third of World's asthma patients. Between 5-11 years of age 10-15% is affected.[4]

In rural children in Delhi, Parental smoking, paracetamol intake, exposure to traffic pollution, exposure to pets were significantly associated with current wheezing whereas in children aged 4-15 years in Chandigarh, a prevalence of 7 percent was observed. [5]

The World Health Organization has estimated that 15 million Disability Adjusted Life Years (DALYs)[6] are lost annually due to asthma, representing 1% of the total global disease burden.Absence from school and days lost from work are reported as substantial social and economic consequence of asthma.

PATHOGENESIS AND PATHOPHYSIOLOGY OF ASTHMA:

Airway inflammation is a major factor implicated in the pathogenesis and pathophysiology of asthma



Air flow limitation in asthma is recurrent and it is caused by variety of changes in airway. The four main pathological changes in asthma are

1. Bronchoconstriction
2. Airway edema
3. Airway Hyperresponsiveness
4. Airway remodeling

1.BRONCHOCONSTRICTION:

The predominant event in asthma is narrowing of air ways, which result in interference with airflow. In acute exacerbations of asthma, bronchial smooth muscle contraction occurs resulting in airway narrowing in response to a variety of stimuli including allergens (or) irritants.

Allergen induced acute bronchoconstriction results from IgE dependent release of mediators from mast cells that include histamine, tryptase, leukotrienes and prostaglandins that directly constrict air way smooth muscles.[7]

In addition other stimuli including exercise, cold and irritants can cause acute air flow obstruction. Stress may also precipitate asthma exacerbation by enhanced generation of proinflammatory cytokines.

2. AIRWAY EDEMA:

As the inflammation becomes more progressive and disease becomes persistent other factors further limit airflow. These includes

Edema

Inflammation

Excess secretion of mucus

Formation of thick mucus plugs

Hypertrophy and hyperplasia of airway smooth muscle

3. AIRWAY HYPERRESPONSIVENESS:

It is an exaggerated bronchoconstrictor response to a wide variety of stimuli. Inflammation is a major factor determining the degree of airway responsiveness. Other factors include structural changes and dysfunctional neuro regulation.

4. AIRWAY REMODELING:

Airway remodeling[8] involves activation of many structural cells which in turn cause permanent changes in the airway that increase airflow obstruction and hyperresponsiveness.

These structural changes include

Thickening of Basement membrane

Sub epithelial fibrosis

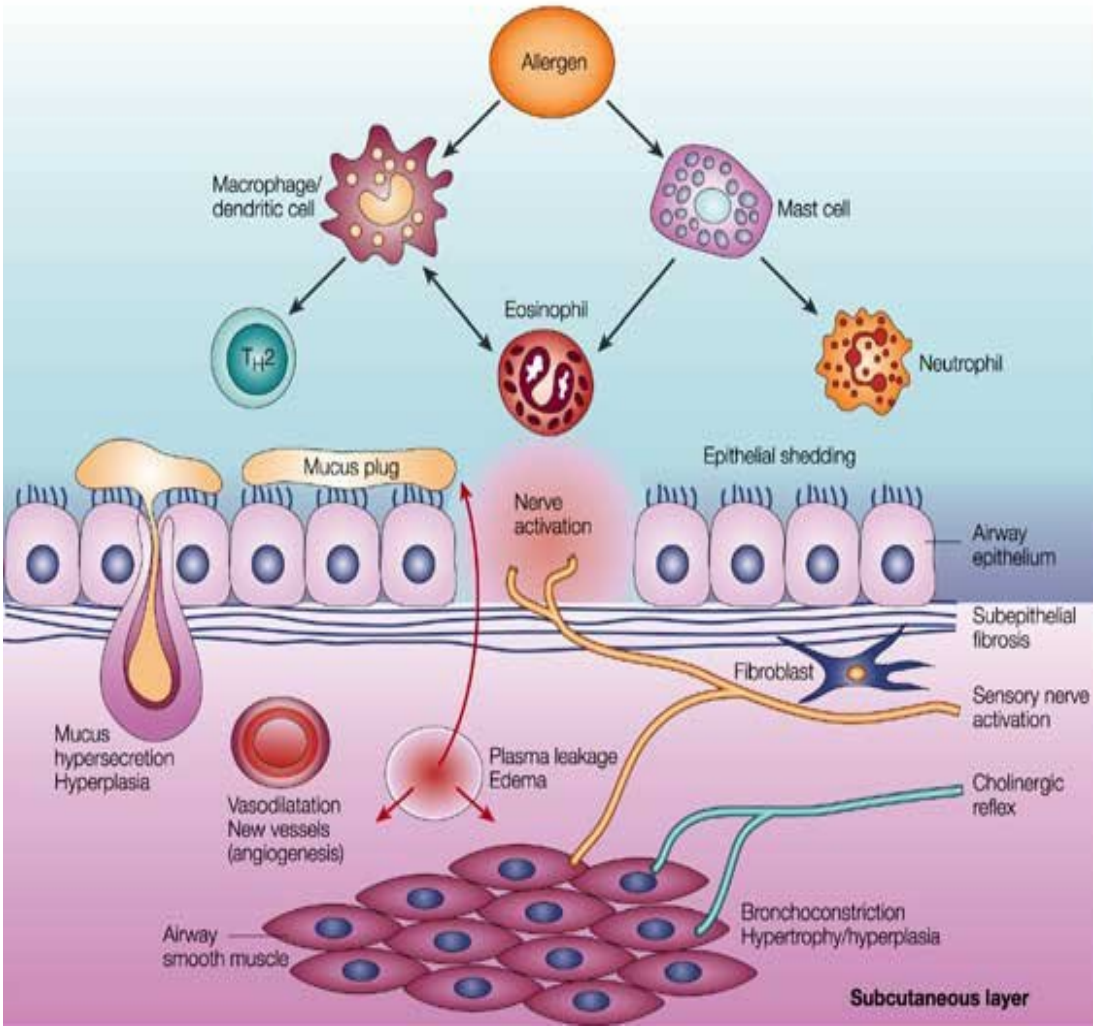
Airway smooth muscle hypertrophy and hyperplasia

Proliferation and dilatation of blood vessels

Mucus gland hyperplasia and hypersecretion.

Therefore the key events involved in persistent nature of the disease and decreased responsiveness to therapy are the process of repair and its regulation. The resulting airway obstruction leads to ventilation perfusion mismatch which in turn causes hypoxemia, hyperventilation or hypoventilation.

Figure 1 PATHOGENESIS OF BRONCHIAL ASTHMA



PATHOPHYSIOLOGIC MECHANISMS OF AIRWAY INFLAMMATION:

Many types of cells and multiple mediators are involved in airway inflammation.

INFLAMMATORY CELLS:

1. LYMPHOCYTES:

There are two subsets of T-lymphocytes, Th1 & Th2. In asthma Th2 plays a major role in generating the cytokines like IL4, IL5 and IL 13.[9] These cytokines are responsible for over production of IgE, Eosinophils and development of airway hyperresponsiveness.

2. MAST CELLS:

Mast cells present in bronchial smooth muscle cells have IgE receptors. Allergens bind to IgE receptors and activate mast cells releasing bronchoconstricting mediators like Histamine, Leukotrienes and Prostaglandins.[10,11,12]

3. EOSINOPHILS:

Almost all of the asthmatics have increased number of eosinophils in their airways. These cells contain inflammatory enzymes, generates Leukotrienes and wide variety of proinflammatory cytokines responsible for airway hyperresponsiveness.[13,14,15]

4. MACROPHAGES:

There are numerous macrophages in airways which have low affinity IgE receptions that may also play a role in inflammatory response.

5. EPITHELIAL CELLS:

Epithelial cells lining the airway epithelium produce more inflammatory mediators when exposed to mediators produced by other inflammatory cells and also by viral infections. This results in epithelial damage worsening the airway obstruction.[16]

INFLAMMATORY MEDIATORS

1. CHEMOKINES:

Chemokines play a role in recruitment of inflammatory cells and are responsible for maintaining the allergic inflammatory response.[17] They are generated by T cells, mast cells, smooth muscle cells, fibroblasts, epithelial cells and endothelial cells. Of the chemokines eotaxin is selective in recruiting the eotaxin. TH2 cells are recruited by activation regulated and macrophage derived chemokines.

2. CYTOKINES:

Cytokines are mediators involved in chronic inflammation of airways even in mildest form of asthma. They are produced by T lymphocytes, eosinophils, epithelial cells, endothelial cells and fibroblasts. Cytokine like IL3 is a mast cell growth factor and stimulates proliferation of eosinophils from bone marrow stem cells. GM –CSF, IL3 and IL5 promote maturation and differentiation of eosinophils. Interferon-γ and IL4 regulate IgE production. They cause selective recruitment and accumulation of eosinophils in the airways by induction of various adhesion molecules. Cytokines act upon inducible nitric oxide synthetase and increase nitric oxide production.

3. CYSTEINYL – LEUKOTRIENES:

These are potent bronchoconstrictors derived mainly from mast cells whose inhibition has been specifically associated with an improvement in lung function and asthma symptoms.[18,19]

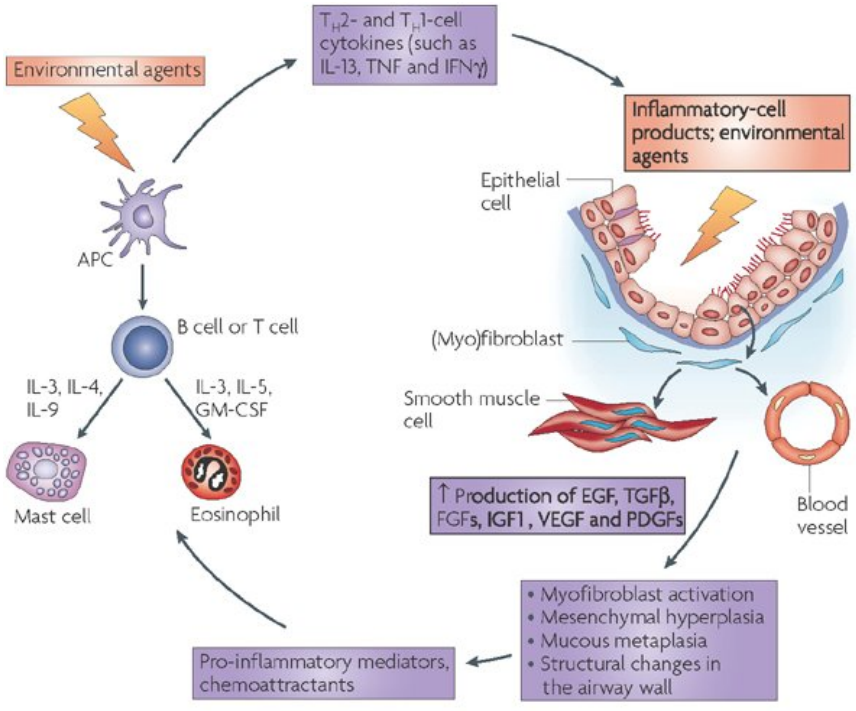
4.NITRIC OXIDE:

It is a potent vasodilator produced by the action of NO synthase in airway epithelial cells.[20,21] NO plays a key role, both in the physiological regulation of the airways and the pathophysiology of asthma. Three forms of NO synthetase act upon aminoacid L - arginine to produce NO endogenously. NO produced by neuronal NOS (nNOS) results in bronchodilatation. NO produced by the endothelial cell NOS (ecNOS) and inducible NOS (iNOS) cause bronchoconstriction by vasodilatation, plasma exudation, mucus secretion and indirect activation of TH2 lymphocytes, worsening the asthmatic inflammatory response.[22] Inducible NOS is inhibited by corticosteroid therapy. Selective inhibition of this enzyme is likely to prove beneficial in the treatment of asthma. Measurements of fractional exhaled NO (FeNO) is useful in monitoring response to asthma treatment.[23]

5.IgE:

IgE is the antibody produced by the plasma cells of lymph nodes. It plays a major role in activation of mast cells and basophils and releasing inflammatory mediators in response to allergen.

Figure 2 PATHOPHYSIOLOGY OF BRONCHIAL ASTHMA



GENETICS OF ASTHMA

Asthma is a disease which has strong genetic predisposition. Maimonides first recognised the familial nature of asthma in the 12th century. Because Asthma runs in families it is likely to be, at least in part linked to genetic factors. Identification of potential candidate genes by the whole genome screen will lead to new and better ways of diagnosis of asthma; identify a particular clinical course and response to therapy. The scope of drug discovery related to products of candidate genes is also widening.

ROLE OF GENETICS IN THE DEVELOPMENT OF ASTHMA:

More than 100 genetic loci[24] have been linked to asthma. Although the genetic linkages to asthma have sometimes differed between cohorts, asthma has been consistently linked with loci containing proallergic, pro inflammatory genes. Genes on chromosomes, 5, 6,11,12,14 seem to be the key players in controlling the inflammatory process in asthma and atopy.[25] Five important genes linked to asthma are PHF11, SPINK5, ADAM33 and GRPA. In addition to these, other genes like IL 13 that alters the production of mucus, FC εR1-β that alter certain innate immune receptors and triggering factors on mast cells have also been identified.

ROLE OF GENETICS IN PREVENTION AND MANAGEMENT OF ASTHMA:

Identification of genes implicated in asthma may lead to classification of asthma in a better way.Recognition of infants and children who are genetically predisposed to asthma would possibly be the initial step in strategies for prevention by environmental or other manipulations in the first year of life.

EARLY CHILDHOOD RISK FACTORS FOR PERSISTENT ASTHMA:

1. Parental Asthma
2. Allergy
    - Atopic dermatitis (eczema)
    - Allergic rhinitis
    - Food allergy
    - Inhalant allergen sensitization
3. Severe lower respiratory tract infection
    - Pneumonia
    - Bronchiolitis requiring hospitalisation
4. Wheezing apart from colds
5. Male gender
6. Low birth weight

7. Environmental tobacco smoke
8. Possible use of acetaminophen (paracetamol)
9. Exposure to chlorinated swimming pools
10. Reduced lung function at birth.[26,27]

SYMPTOMS OF ASTHMA

Recurrent isolated cough

Recurrent Wheeze, Recurrent breathlessness

Night time cough

Tightness of Chest

Cough or Wheeze induced by exercise.

The symptoms of asthma usually occur during the night time. This may be attributed to the hormonal changes that take place during later part of the night or early morning. The Serum cortisol and epinephrine levels reach nadir in early morning causing increased airway resistance and nocturnal symptoms.

EARLY WARNING SIGNS OF ASTHMA:

Increased breathing through mouth during sleep

Increased cough at night

Feeling restlessness during sleep

Increased tiredness during activities

Worsening of symptoms like cough, wheeze or running nose during exercise.

TYPES OF CHILDHOOD ASTHMA

There are two main types of childhood asthma.

1. Recurrent Wheezing
2. Chronic asthma

RECURRENT WHEEZING:

Recurrent wheeze occur in children less than 3 years. This may be due to some viral infections of the respiratory tract that occur during childhood and also because of decreased lung function in newborn period. As lung function improves with age wheeze will not recur.

CHRONIC ASTHMA:

This type of asthma is associated with allergy that persists into later childhood and often adulthood.

NON ATOPIC WHEEZE:

If Wheezing recur, after 3yrs of age it is called persistent wheeze. The most important cause for this wheeze is respiratory infections caused by viruses like RSV. These Viral infections can cause increased tone of smooth muscles in the respiratory tract which can improve with age.

ATOPIC WHEEZE:

This type of Wheeze occurs in children with atopy. It is of two types namely early atopic Wheeze and late atopic Wheeze.

These children are susceptible to various allergens leading to hypersensitivity of their airways and obstruction. Children with repeated exposures to triggering factors easily develop asthma in their adulthood.

Moral Gil et al[28] revealed that non atopic or transient wheeze was classified as non-allergic type of asthma.

But Taussig et al[29] in his study mentioned that asthma in children which is caused by many factors cannot be grouped into any type.

O' Connell et al[30] reported that, wheezing in children of 8 years of age with hypersensitivity and smoking history in the family was 28 times

more than normal children. Recently, environmental factors have found to play an important role in allergic asthma when compared to genetic factors.

TRIGGERS OF ASTHMA

Asthma symptoms are triggered by many factors such as allergies and activities.

ENVIRONMENTAL FACTORS:

1. ALLERGENS:

Indoor: Domestic mites, furred animals, dogs, cats, mice) cockroach allergens, fungi, moulds, yeast.[31, 32]

Outdoor: Pollens, fungi, moulds, yeast

2. Infections (especially viral)
3. Occupational sensitizers
4. Tobacco smoke
5. Outdoor / Indoor air pollution
6. Food allergy

HOST FACTORS:

i) Genetic

(1) Genes predisposing to atopy

(2) Genes predisposing to airway hyperresponsiveness

ii) Obesity

iii) Sex

Around Eighty percent of people with asthma have allergies to airborne substances, such as tree, grass, weed pollens mold, animal dander, dust mites etc. It has been found that children who had high levels of cockroach droppings in their homes were four times likely to have childhood asthma than children who had low levels of these droppings at home.[33, 34]

FOOD AND FOOD ADDITIVES THAT TRIGGER ASTHMA:

Allergies to food can lead to mild to severe life threatening reactions. Some of the most common foods associated with allergic manifestations are

Eggs

Peanuts

Fish, Shell fish

Cow's milk

Wheat

Salads & fresh fruits,

Food preservatives can also trigger asthma in those children who are sensitive. These include Sodium bisulfite, Potassium bisulfite, Sodium meta bisulfite, potassium meta bisulfite and sodium sulfite.

ASTHMA & COLD AIR

Changes in Air temperature provoke symptoms of asthma. Going from a warm room into cold air outside triggers allergic symptoms.

ASTHMA AND DRUGS:

Certain drugs also trigger asthma symptoms. These include aspirin, beta blockers NSAIDS such as Ibuprofen.

OTHER TRIGGERS:

Paint fumes

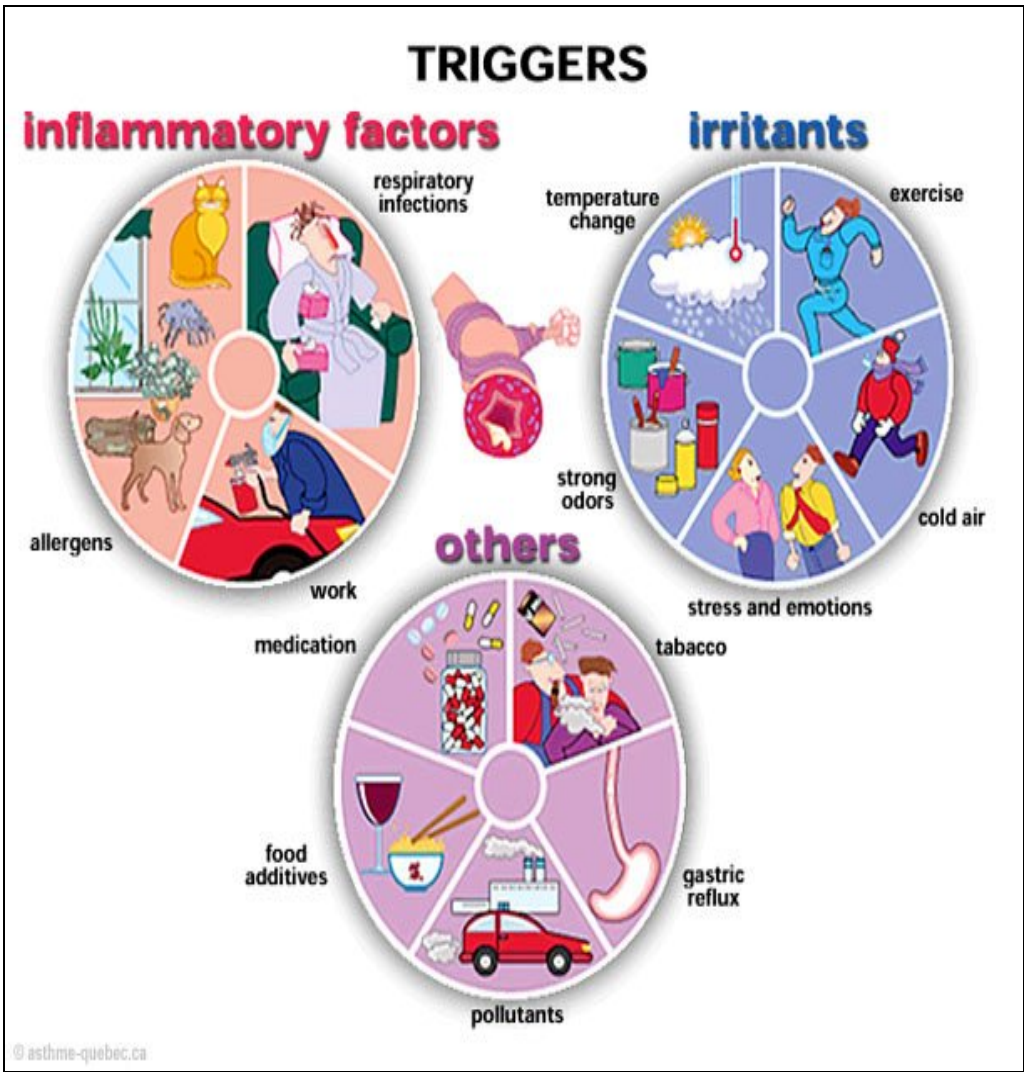
House hold chemicals such as those found in air fresheners

Perfumed cosmetics

Strongly scented flowers

Exercise and Emotions.

IGURE 3 TRIGGERS OF ASTHMA



OBESITY:

Obese individuals are more at risk of developing asthma. How obesity promotes the development of asthma is unclear. Obese patients have a reduced expiratory reserve volume which may alter airway smooth muscle plasticity and airway function. Furthermore release of proinflammatory cytokines and mediators such as Interleukin 6, TNF-α, eotaxin and leptin by adipocytes combined with a lower level of anti inflammatory adiopkines in obese subjects can favor a systemic inflammatory state.[35-37]

IgE IN BRONCHIAL ASTHMA:

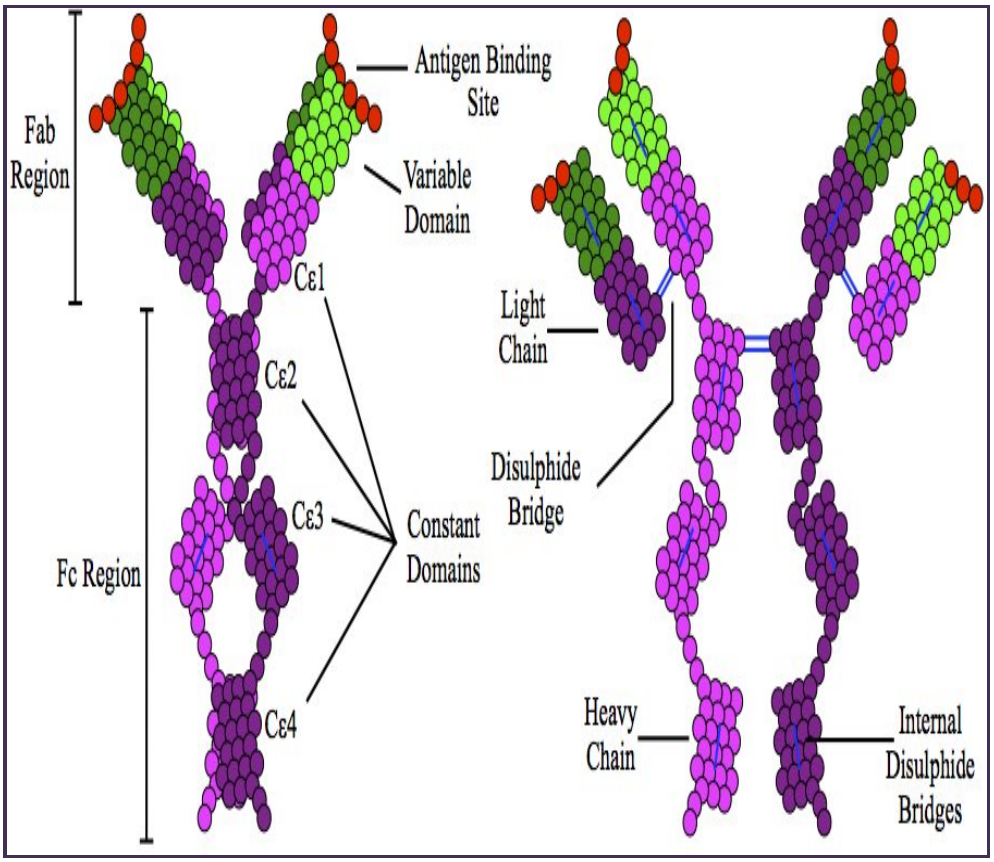
IgE is a class of antibody (or) immunoglobulin found only in mammals. It was discovered in 1966 by Japanese scientist Teruko and Dikimishiga – Ishizaka. IgE is produced by plasma cells and B lymphocytes in airway, regional lymph nodes and gastrointestinal tract. It comprises only 0.001% of circulating immunoglobulin. Normal IgE levels ranges from 0 -230 IU/ml in male children and 0 – 170 IU/ml in female children.[38]

IgE plays an essential role in type I hypersensitive reactions which manifest various allergic diseases like asthma, allergic rhinitis, food allergy, urticaria and atopic dermatitis. It mediates the allergic response

by binding to Fc receptors, found on surface of mast cells and basophils.[39-42]

Binding of IgE to mast cells initiate an allergic cascade.

FIGURE 4 STRUCTURE OF IgE



STEPS INVOLVED IN ALLERGIC CASCADE:

Sensitization to an allergen

Early phase reaction

Last phase reaction.

1. SENSITIZATION TO AN ALLERGEN:

In susceptible individuals, the first step in developing an allergic reaction is repeated exposures to a particular antigen. Some allergens cause mild reactions and some can trigger strong allergic reaction.

Allergens induce the T cells which then activate B cells. Activated B cells get transformed into plasma cells. These plasma cells are capable of producing and releasing more antibodies.

EARLY PHASE REACTION:

This phase begins with binding of IgE to mast cells, which occurs within half an hour after initial exposure. IgE mediates allergic response by binding to specialized receptors called Fc receptors on the surface of mast cells and basophils. Fc receptors are of two types, Type I and Type II.

Type I Fc receptors are high affinity IgE receptors, found in basophils and mast cells. Type II receptors also known as CD23 are low affinity IgE receptors found in B cells,macrophages , eosinophils and

platelets.When a substantial mass of IgE binds to mast cells, it release histamine and other inflammatory mediators and initiates the allergic reaction.[43]

LATE PHASE REACTION:

It usually begins at the same time as early phase reaction but the symptoms manifest some 3 to 10 hours later. This phase involves immune cells such as eosinophils. During this phase the symptoms become more severe than those seen during the early phase and it also lasts for 24 hours (or) more before subsiding.[43]

CONSEQUENCES OF CHRONIC ALLERGY AND REACTION IN ASTHIMA

Repeated exposures to an allergen and subsequent allergic reaction leads to airway hyperresponsiveness and airway remodeling. These changes can cause permanent damage to the airway. Long term controller medications that significantly reduce airway inflammation and maintain maximum lung function can lessen the risk of permanent damage.

DIAGNOSIS OF ASTHMA

PULMONARY FUNCTIONS TESTS

Pulmonary function test is one of the basic tool in evaluating a patient's respiratory status. In day to day practice the common lung function tests used to diagnose asthma are spirometry and peak expiratory flowmetry. These tests are usually preformed in children above 5-6 years of age.[44]

SPIROMETRY:

Spirometers are instruments used for spirometry and spirogram is the tracing generated by the spirometer. Spirometry provides an objective assessment of air flow obstruction and is useful in the staging of asthma according to severity. It is used to measure the maximal expiratory effort following maximal inhalation.[45]

The four indices that are mainly used to interpret spirometry are forced vital capacity (FVC), forced expiratory volume (FEV1), forced expiratory ratio (FEV1/FVC) and forced expiratory flow (FEF). In Asthma the forced expiratory volume in 1 second (FEV1) is usually decreased, the forced vital capacity is usually normal and the ratio FEV1/FVC is decreased.

The success of spirometry depends mainly in producing an acceptable and reproducible FVC curve. Only with adequate training and encouragement, children above 5-6 years can produce an acceptable FVC curve.

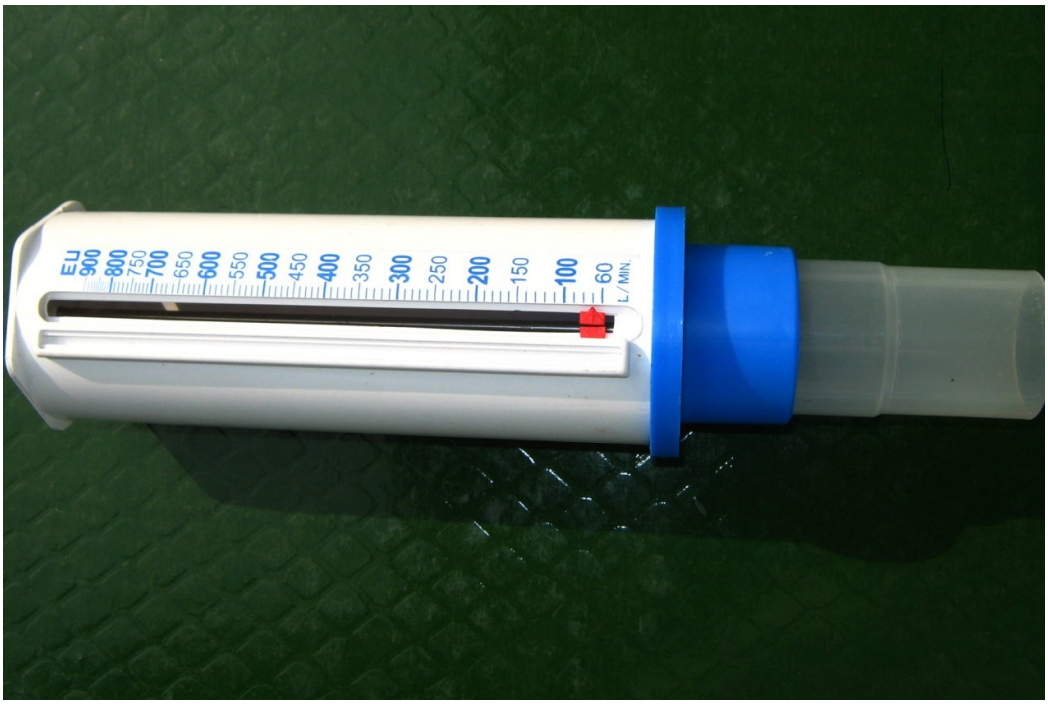
PEAK EXPIRATORY FLOW METRY:

Peak flow meter is a portable, handy device, used to measure peak expiratory flow rate. It can be easily and accurately performed by children more than 5 years. It is useful in the diagnosis and monitoring of asthma patients regularly .Children with Asthma can use this device at home to record and monitor their peak flow rate.[46,47,49]

Peak expiratory flow rate is the maximum flow rate generated during a forceful exhalation after maximal inspiration. It correlates with FEV1 in spirometry.

The PEFR reading is correlated with the predicted values from standard normogram based on height of the child. The formula used to calculate PEFR,

5 PEAK FLOW METER



6 CHILD PERFORMING PEAK FLOW METRY

PEFR = [(Ht in cms -100) x 5] +100

PEFR values <80% of predicted values are considered abnormal.

Further confirmation can be done by a bronchodilator reversibility test.>20% improvement in recording after giving a bronchodilator confirms reversible bronchospasm.[48-50]

A diurnal variation in PEFR of >20% is also an indicator of asthma.

EXERCISE TEST:

PEFR is recorded following a vigorous exercise for 5-6 minutes. A fall in PEFR by at least 15% at the end of the test is useful in diagnosing exercise induced asthma.

METHACHOLINE CHALLENGE TEST:

The presence of airway hyperresponsiveness can be determined by Methacholine bronchial provocation challenge. In this procedure patients are allowed to inhale increasing concentrations of Methacholine. Methacholine is a cholinergic agonist which acts by stimulating the muscarinic receptors on smooth muscle cells in the airway to cause constriction.

Patients with asthma are more sensitive to methacholine than normal individuals. The smooth muscles in their airway constricts at

lower concentrations of this medication. The results of this test are typically expressed as a provocative concentration of methacholine that causes 20% of decline in FEV1 (denoted as PC 20). A methacholine PC20 of less than 8mg/dl has sensitivity of 100% for asthma. A PC20 between 2 and 8 mg/dl is considered mild asthma. It is a more clinically useful tool to exclude the diagnosis of asthma.[51-53]

EXHALED NITRIC OXIDE:

Exhaled Nitric Oxide is an inflammatory by product which is elevated in asthmatics. In 1991, the nitric oxide was first identified in breath samples that are exhaled. In 1993, exhaled Nitric Oxide (eNO) was reported in asthmatics by researchers from Sweden. It can be elevated in atopy alone and is not always an indicator of asthma.

However exhaled nitric oxide (FeNO) is used as a diagnostic tool for asthma in corticosteroid sensitive patients and it is rapidly reduced by inhaled corticosteroids. Patients with FeNO guided inhaled corticosteroid therapy have good level of asthma control achieved at lower doses of corticosteroid.[54,55]

Hence FeNO may be useful in providing an indication of corticosteroid sensitivity, monitoring asthma control and guiding therapy in corticosteroid responsive cases.

SKIN PRICK TEST (ALLERGY TESTING):

Skin Prick Test is quiet reliable, rapid and cost effective that is useful in determining the triggers of asthma. In this test the IgE medicated responses are identified by injecting particular antigens into the skin. These antigens trigger mast cells in children with allergies. Activated mast cells release mediators like histamine which can induce itching, swelling and redness. A wheal of 3mm (or) more in diameter is considered as positive. These tests will be helpful in effective management of asthmatic children by avoidance of specific allergies.[56]

GLOBAL INITIATIVE FOR ASTHMA (GINA) GUIDELINES FOR ASSESSING SEVERITY:

The global initiative for Asthma was formed in 1993. Its goals and objectives were described in a 1995 NHLBI / WHO workshop report, global strategy for Asthma, Management and prevention.

In 2002 guidelines were phrased based on severity of Asthma. Patients were graded into intermittent, mild, moderate and severe grades of asthma based on these guidelines.[57,58]

Table 1 Grading of Asthma

SEVERITY	INTERMITTENT	PERSISTENT		
		MILD	MODERATE	SEVERE
DAY SYMPTOMS	< 1 per week	≥ 1 per week	Daily Affects daily activities	Daily Limits daily activities
NIGHT SYMPTOMS	≤ 2 per month	≥ 2 per month	>1 per week	Frequent
PEF	≥ 80% predicted	≥ 80% predicted	>60 <79% predicted	<60% predicted
PEF VARIABILITY	≤ 20%	20 - 30%	>30%	>30%
FEV1	≥ 80%	≥ 80%	60 -79%	<60%

MANAGEMENT OF ASTHMA

GOALS OF ASTHMA THERAPY:

- To prevent chronic and troublesome symptoms i.e., cough, breathlessness in the night, early morning (or) post exertion.
- To minimize the frequent need of quick reliever medications.
- To maintain near "normal" pulmonary function.
- To maintain normal activity levels including physical activity and school attendance.
- To prevent recurrent exacerbations and minimize the need for emergency visits and hospitalization.
- To provide optimal therapy with minimal or no adverse effects.
- To meet patients and families expectations of and satisfactions with asthma care.

The choice of initial therapy is based on assessment of asthma severity, and for patients who are already using controller therapy, modification of treatment is based on assessment of asthma control and responsiveness to therapy.

Persistent asthma is most effectively controlled with daily anti inflammatory therapy. Under diagnosis and inappropriate therapy are major contributors to asthma morbidity and mortality.

LONG TERM CONTROLLER MEDICATIONS:

Long-term medications for control are used to achieve and maintain control of persistent asthma.

These include

1. Corticosteroids
2. Long acting inhaled –β agonist
3. Leukotriene modifiers
4. Non-steroidal Anti-inflammatory agents
5. Methylxanthines

INHALED CORTICOSTEROIDS:

Inhaled corticosteroid therapy has been shown to improve lung function, as well as to reduce symptoms, AHR and use of rescue medications.It has been found to reduce emergency care visits and hospitalizations by about 50% .The NIH guidelines recommend daily ICS therapy as the treatment of choice for all patients with persistent asthma. ICS therapy may lower the risk of death due to asthma. These are

available as metered-dose inhalers (MDIs), dry powder inhalers (DPIs) or as suspension for nebulisation.

The currently used ICS in asthma are Budesonide, fluticatosone propionate and beclomethasone.[59-63]

SYSTEMIC CORTICOSTEROIDS:

Oral corticosteroids are used primarily to treat asthma exacerbations and rarely in patients with severe disease who remain symptomatic despite optimal use of other asthma medications. Predinisolone and methyl predinisolone are steroids that are used orally.

LONG-ACTING INHALED β-AGONISTS:

These are long acting bronchodilators used concomitantly with anti-inflammatory drugs to achieve long term control, especially nocturnal symptoms. They are not used as rescue medications for acute asthma symptoms or exacerbations, nor as monotherapy for persistent asthma. LABs major role is, as an add on agent in patients whose asthma is sub optimally controlled with ICS therapy alone. Several studies have found that addition of an LAB to ICS therapy to be superior to doubling the dose of ICS, especially on day and night symptoms.[59,63,65]

LEUKOTRIENE MODIFIERS:

Leukotrienes are potent pro-inflammatory mediators that can induce bronchospasm, mucus secretion and airway edema. There are two types of Leukotriene modifiers.

1. Leukotriene synthesis inhibitors
2. Leukotriene receptor antagonists (LTRAs)

Zileuton, the only leukotriene synthesis inhibitor is not approved for use in children <12 years of age. LTRAs have bronchodilator and targeted anti-inflammatory properties and reduce exercise, aspirin and allergen induced bronchoconstriction. They are recommended as alternative treatment for mild persistent asthma and as add-on medication with ICS for moderate persistent asthma.

Two LTRAs that are FDA approved for use in children are montelukast and Zafirlukast. Montelukast is used for children > 1 year of age and Zafirlukast is used in children >5 years of age.[64]

NON STEROIDAL ANTI INFLAMMATORY AGENTS:

Cromolyn and nedocromil are NSAIDS that may be used as initial choice for long term control. It is also used as preventive therapy prior to exercise (or) unavoidable exposure to known allergens. They can be used in place of SABAs especially in children who develop unwanted effects with β-agonist therapy.

METHYLXANTHINES:

Sustained release theophylline is a mild to moderate bronchodilator used as an adjuvant to inhaled corticosteroids for prevention of nocturnal symptoms. It may also have anti inflammatory effects. When used long term, theophylline can reduce asthma symptoms and the need for rescue SABA use.[66]

QUICK RELIEF MEDICATIONS:

Quick Relief medications are used to treat acute symptoms and exacerbations.

It includes

1. Short acting inhaled β-agonists.
2. Anticholinergics
3. Systemic corticosteroids

SHORT ACTING INHALED β-AGONISTS

SABAs like Albuterol, Levalbuterol, terburtaline, pirbuterol are the drugs of choice for acute asthma symptoms and preventing exercise induced bronchospasm. β-Agonists cause broncodilation by inducing airway smooth muscle relaxation, reducing vascular permeability and airway edema and improving mucociliary clearance.

ANTI CHOLINERGIC AGENTS:

Inhaled Ipratropium is used primarily in the treatment of acute severe asthma. It is proving to be of immense value in infant wheezers and severe persistent asthmatics. But they are much less potent that β-Agonists.

SYSTEMIC CORTICOSTEROIDS:

Used in moderate to severe exacerbations to speed recovery and prevent recurrence of exacerbations.

ANTI –IgE THERAPY IN ASTHMA:

As IgE plays a major role in type I hypersensitivity reactions, it has been found out that any means of reducing circulating levels of IgE would be helpful in the treatment of allergic diseases especially asthma.

IgE exerts its effect by binding to high affinity Fc epsilon receptors on mast cells, eosinophils and basophils. These receptors are also found in Dentritic cells particularly type II dentritic cells which support Th2 responses.

Omalizumab is a newly discovered recombinant humanized monoclonal antibody. It acts by preventing the binding of IgE to high affinity receptors and initiation of allergic immune response. Treatment with this drug has resulted in noticeable reduction in free IgE levels and also down regulation of IgE receptors on dentritic cells and basophils.

Omalizumab has showed promising results in the treatment of moderate to severe allergic asthma by reducing exacerbations and need for corticosteroid. In a double blind, parallel multicenter study, it was shown that Omalizumab was successful in the treatment of difficult to treat asthmatics as add on therapy.[67-69]

Several studies have also revealed that this drug has altered the cytokine levels as well as number of Fc epsilon receptors (or) IL4 cells and also reduced airway eosinophilia.

MEPOLIZUMAB:

It is a newly introduced anti-interleukin 5 antibody which has shown to improve asthma control, reduce predinisolone dose and lower sputum and blood eosinophil events in adults with prednisone dependent asthma who also had sputum eosinophils.[70]

ROLE OF BREAST FEEDING IN ASTHMA:

It was shown that prolonged breast feeding could reduce the risk of allergic and respiratory diseases. There are numerous studies which have shown that exclusive breast feeding for a period of at least 3 months have protective effect in the development of asthma and other allergic diseases.

In a cross sectional study conducted in 1500 infants from well baby clinic & pediatric clinics in the state of Qatar from October 2006 to September 2007, more than half of the infants (59.3%) were exclusively breastfed, 28.3% were partially breastfed and 12.4% were artificially fed. The incidence of Asthma (15.6%), wheezing (12.7%), Allergic rhinitis (22.6%) and eczema (19.4%) were found to be lower in exclusively breastfed children. The risk of allergic diseases were found to be lower particularly in children with prolonged breast feeding > 6 months than in those children who are breastfed for short term (<6 months).[71,72]

STRATEGIES FOR AVOIDING COMMON TRIGGERING FACTORS:

1. Children should stay away from tobacco smoke. Parents and relatives should be advised not to smoke at least indoor.
2. Drugs, foods and additives that are known to precipitate symptoms of asthma should be avoided.
3. Bed linens and blankets must be washed weekly in hot water and dried in a hot dryer or the sun.
4. Pillows and Mattresses should be encased in air-tight cover.
5. Carpets must be replaced with hard flooring especially in sleeping rooms.
6. Pet animals should be removed from the home (or) at least from the sleeping area.
7. House should be cleaned thoroughly and frequently.
8. Pesticide spray can be used to avoid cockroaches.
9. Windows and doors should remain closed when pollen and mould counts are highest.
10. Any damp area in the home should be cleaned frequently.

AIM OF THE STUDY

AIM OF THE STUDY

1. To assess the severity of Asthma clinically and by peak flow metry.

2. To estimate serum IgE levels in Asthmatic children.

3. To compare the serum IgE levels in mild, moderate and severe grades of Asthma.

4. To study the association of various epidemiological factors to severity of asthma.

NATURE OF STUDY:

Case Study

PLACE OF STUDY:

Govt. Mohan Kumaramangalam Medical college hospital, Salem – 636001

PERIOD OF STUDY:

October 2011 to September 2012

INCLUSION CRITERIA:

Children between 5-12 years of age and both sexes with symptoms and signs suggestive of asthma.

EXCLUSION CRITERIA:

1. Asthmatic who had taken bronchodilator with in 24 hrs prior to assessment.
2. Chronic respiratory diseases other than asthma
3. Children with history suggestive of worm infestation.
4. Immunocompromised children.

MATERIALS AND METHODS

MATERIALS AND METHODS

The study population included 75 children from those attending the outpatient as well as those admitted in the department of pediatrics of Government Mohan Kumaramangalam Medical College Hospital, Salem with symptoms and sign suggestive of bronchial asthma.

Detailed history was taken regarding patients name, age, sex, duration, frequency of symptoms and severity of exacerbations. All cases were provided with a respiratory questionnaire which included questions on respiratory symptoms, passive smoking, family history and previous medical history. Age and sex matched 75 healthy volunteers were taken as control group.

The study was approved by ethical committee and informed consent was obtained from all cases and controls. Peak flow metry was carried out in all children, as there was difficulty in obtaining an acceptable FVC curve by spirometry. Severity of asthma was assessed by clinical history and peak flowmetry. The cases were categorized into intermittent, mild, moderate and severe grades of asthma based on global initiative for Asthma guidelines 2002.

After taking necessary aseptic precautions, blood samples were collected from each patient. The samples were left undisturbed for about half an hour to allow for clot formation. After complete formation of clot, the samples were centrifuged to separate the serum. The centrifuged samples were stored at -20 ^{0}C till the analysis was done.

Using Pathozyme Omega Diagnostics IgE Elisa kit, serum IgE levels were measured.

PRINCIPLE OF THE TEST:

Test sera were applied to specific monoclonal anti IgE antibody coated micro titration wells and incubated with Zero buffer. When human IgE is present in the test sample, it will combine with the antibody on the well. Residual test sample and IgE antibody are washed with the addition of Horse radish peroxidase enzyme. IgE molecules get sandwiched between the enzyme linked antibodies and solid phase. When a substrate is added, those wells with IgE produce a colour absorbance which is measured at 450mm. The concentration of IgE is directly proportional to the intensity of colour.

STATISTICAL ANALYSIS:

Is done by Kruskal Wallis H test for two groups (equivalent to chi-square test) The Kruskal–Wallis test is most commonly used when there is one nominal variable and one measurement variable, and the measurement variable does not meet the normality assumption of an ANOVA (analysis of variance). If the original data set actually consists of one nominal variable and one ranked variable, you cannot do an anova and must use the Kruskal–Wallis test.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

THIRUNAVUKARASU – et - al

In a cross sectional study done by Thirunavukarasu et al,[73] Serum IgE levels were estimated in asthmatics and normal subjects between 18 - 60 years of age. They compared the values between various grades of asthma and also with control groups. In normal subjects the mean IgE level was 151.95 IU/ml and in severe asthmatics it was 1045.32 IU/ ml. They reported that serum IgE levels were high in asthmatics as compared to normal subjects and also the IgE levels increased as the severity of asthma increased. Though the IgE levels differed significantly with severity of asthma it does not completely explain the severity of symptoms and signs. They concluded that there are other factors like cytokines which may explain the severity.

ANUPAMA et al

Anupama et al[74] also studied the association of serum IgE levels with the magnitude of asthma in adults. Their study group included 132 patients and 30 healthy controls between 15 – 60 years. The cases were categorized in to mild, moderate and severe grades based on history and pulmonary function tests. Using chemiluminescence automated system

the serum IgE levels of the study group was estimated. The average IgE levels in control groups, mild, moderate and severe grades of asthma were 127.5±2.9 IU/ml, 212.3 ±9.8 IU/ml, 489.2 ±5.4 IU/ml & 1059.6 ±5.9 IU/ml respectively. The values correlated significantly with the severity of asthma. They reported that in bronchial asthma the IgE levels are elevated substantially and also it reflected the severity.

According to them the extent of inflammation and obstruction of airways are related to serum IgE concentrations in asthmatics.

HOGARTH et al

In a Longitudinal epidemiological study of asthmatic and wheezing school children in Melbourne by Hogarth et al[75] showed that serum IgE levels increased in association with increasing frequency and severity of asthma. However in this study some controls and mild asthmatics showed significant elevation in their serum IgE levels, while some severe asthmatics had normal (or) very low levels of IgE. They came to the conclusion that IgE effects its clinical manifestations in cell-associated state, rather than as free antibody in the plasma.

SUNYER et al

Sunyer et al[76] analysed the relationship between Total serum IgE levels and asthma independent of specific IgE levels to frequent environmental allergens. Their sample size consisted of 1,961 symptomatic individuals aged 20 – 24 years. Total and specific serum IgE levels to moulds, pets and mites were estimated. They found that patients with recent symptoms of asthma showed strong association with Total IgE levels.

There was an association between asthma and total IgE even in individuals without specific IgE antibodies. They concluded that this association could indicate the allergic nature of asthma even in non – atopic persons.

MEHMET et al

Mehmet et al[77] compared the total serum IgE levels with multiple risk factors associated with allergy in children with asthma. In their study, 140 children (49 female, 91 male) of 3 – 15 years with asthma were included. Total IgE was found to be high in males compared to females ($p = 0.03$). Serum IgE concentrations correlated well with passive smoking ($r = 0.40$, $p = 0.03$), absolute eosinophil count ($r = 0.46$, $p = 0.01$) and number of house hold members ($r = 0.41$, $p = 0.02$). But they found that

there was no significant association between breast feeding duration, cow's milk feeding and duration of disease to total IgE levels. They finally reported that in children with asthma, the serum IgE levels are associated with various factors like sex, crowded family and passive smoking.

MELISSA et al

In a longitudinal study by Melissa et al[78] the interaction between pediatric asthma and parent and grandparent status was analyzed. In this study children who had a parent with asthma were twice (OR = 1.96) more likely to have asthma, compared to those children who had a parent without asthma. The chances of asthma was 4 times more in children who had parents as well as grandparents with asthma (OR = 4.27). They reported that family history played a significant role as a predictor of doctor diagnosed asthma regardless of socio economic status and ethnicity.

SHAHID SUKHBIR

A prospective descriptive study was conducted in wheezing children between 0-12 years by Sukhbir[79]to analyse the impact of passive smoking with the age of onset and severity of wheezing.

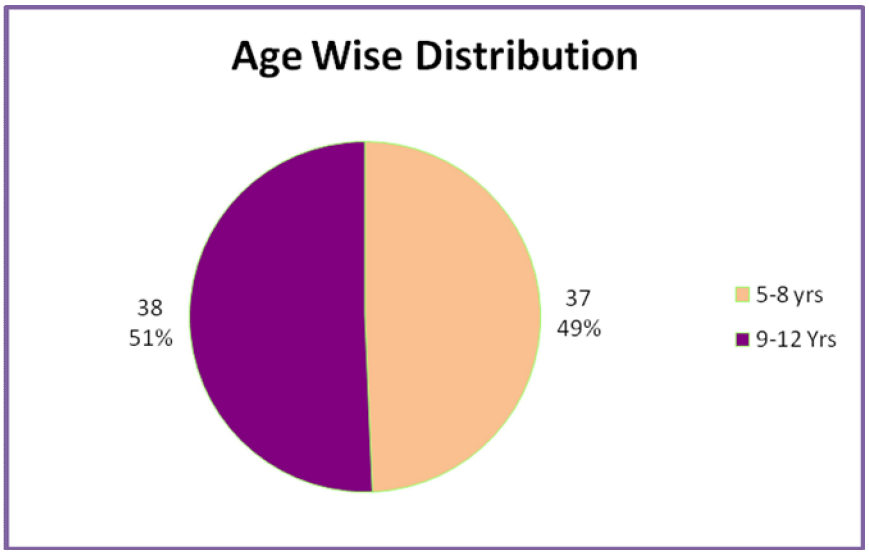
He found that children who had exposure to house hold tobacco smoke had early onset and severe wheeze compared to children who did not have exposure to passive smoking.

HARRY HERRICK

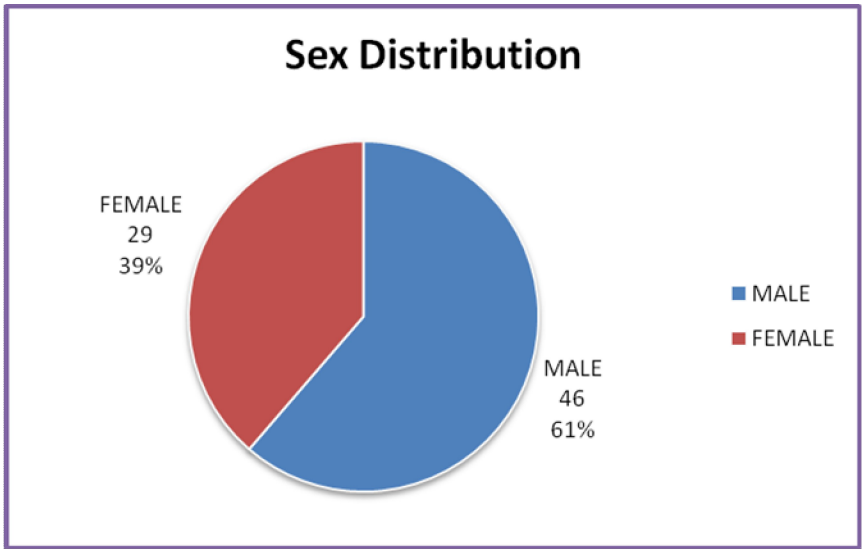
Harry Herrick[80] studied the association of duration of breast feeding and incidence of asthma in children. According to this study children who were never breastfed or breastfed for less than 3 months were found to develop symptoms of asthma at an earlier age.

RESULTS

RESULTS



Number of cases in the age groups of 5-8 years and 9-12 years were almost same.

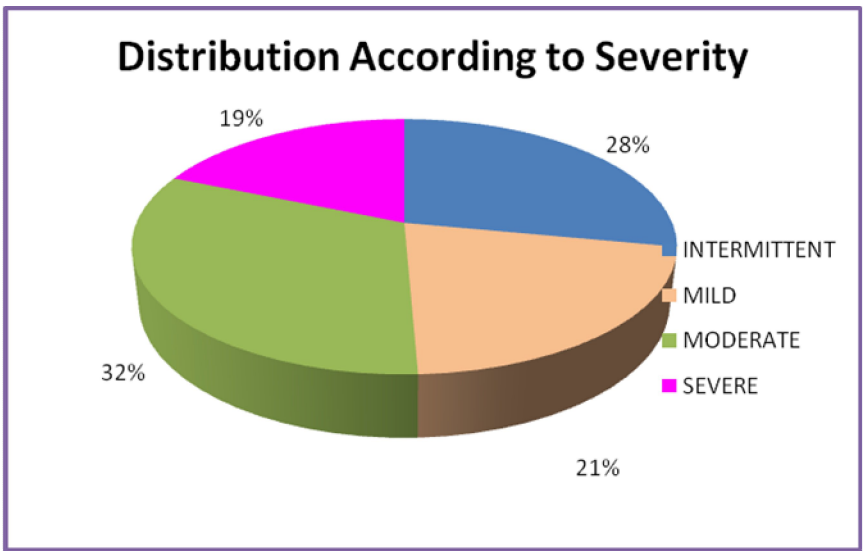


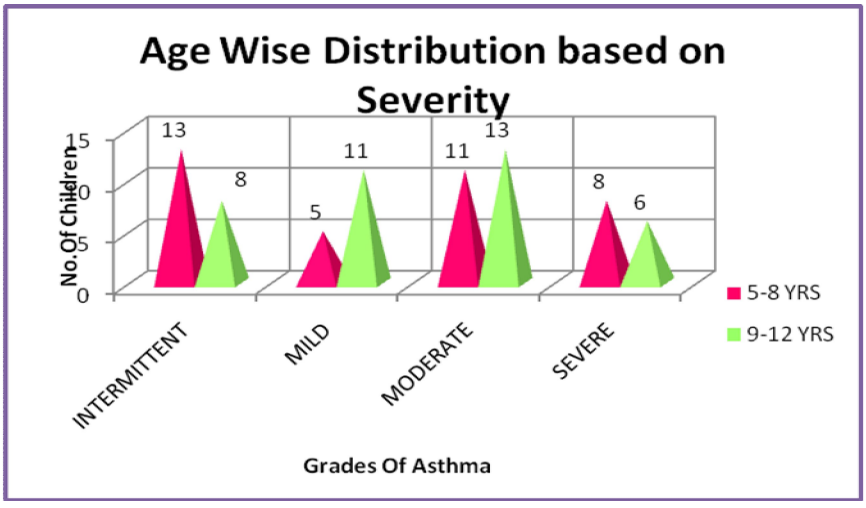
Maximum numbers of cases were male children.

Table 2 Distribution According to Severity

Severity of Asthma	No. of cases	Percentage
Intermittent	21	28%
Mild Persistent	16	21%
Moderate persistent	24	32%
Severe persistent	16	19%
Total	75	100%

Majority of asthmatic children belong to moderate persistent category.



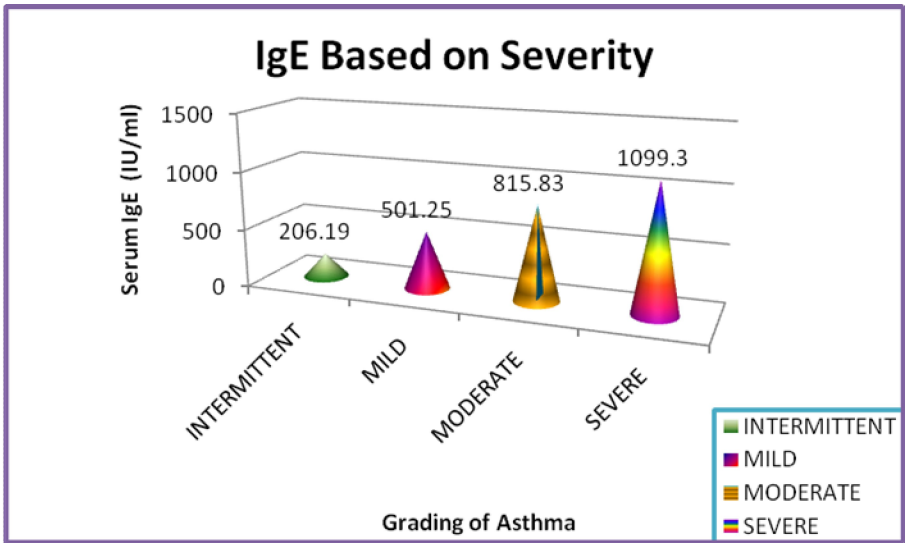


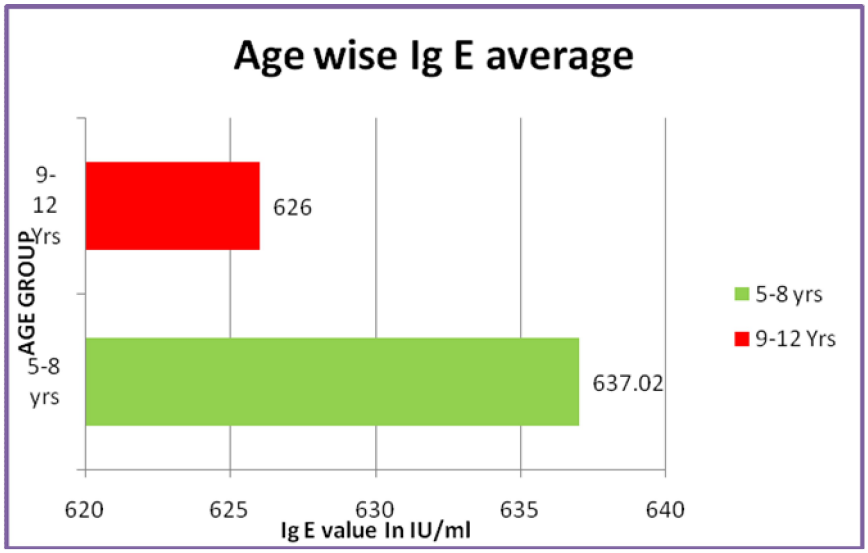
Majority of cases in 5-8 years belong to Intermittent category and in 9-12 years maximum number of children where in Moderate persistent category.

Table 3 Serum IgE levels in Control groups and Cases

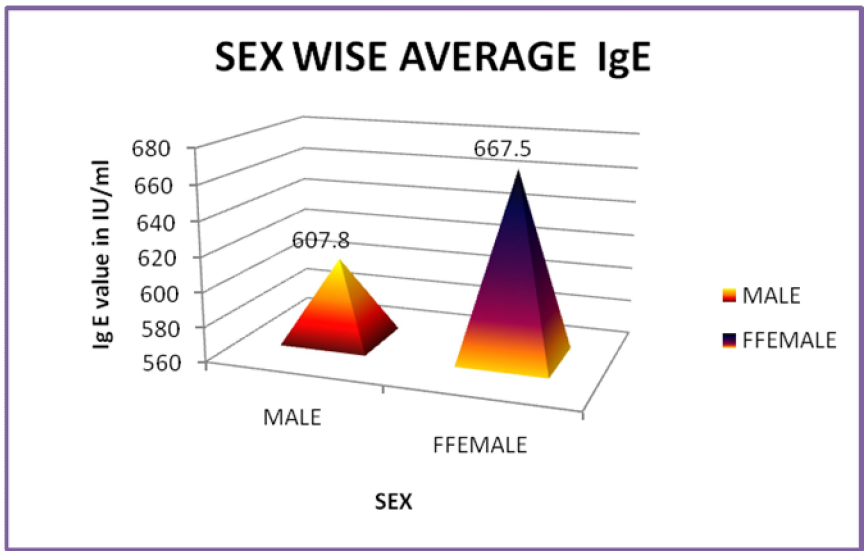
Groups	No. of cases	Average IgE (IU/ml)
Control	75	89.90
Intermittent	21	206.19
Mild	16	501.25
Moderate	24	815.83
Severe	16	1099.3

IgE levels were elevated in cases compared to controls. Severe asthmatics had high serum IgE levels and low levels were found in Intermittent category.





The serum IgE levels did not differ significantly in both age groups.

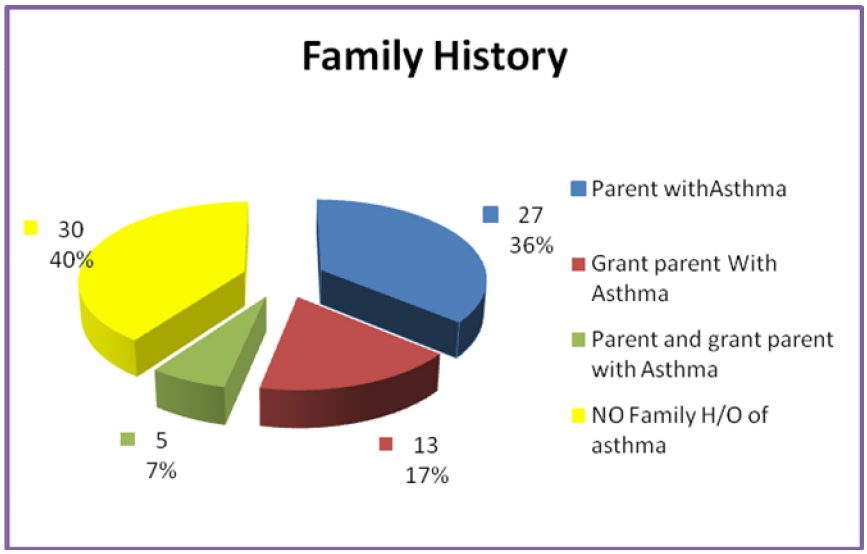


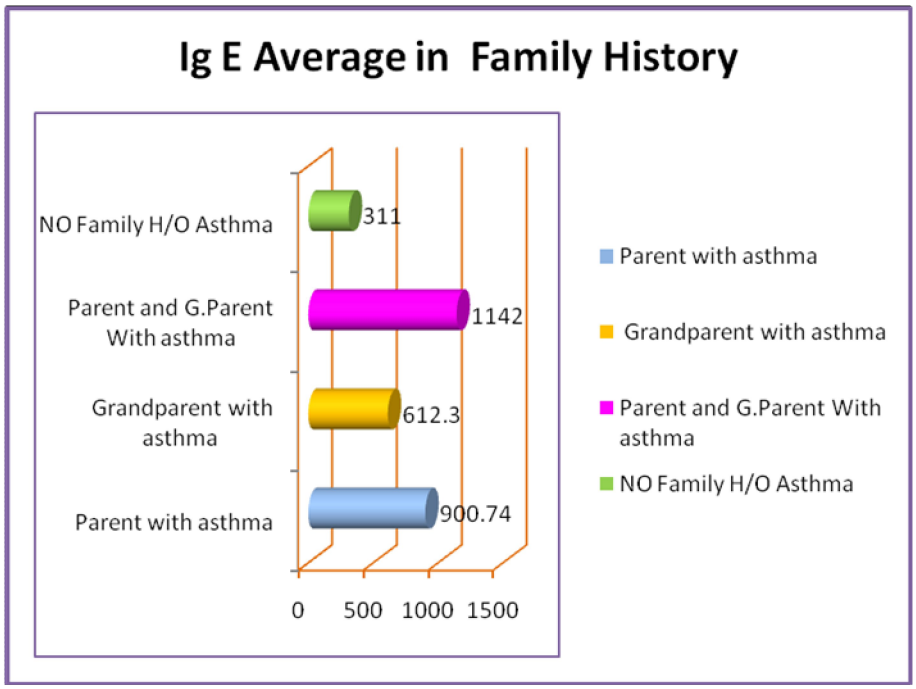
The average IgE levels in both sexes did not vary significantly.

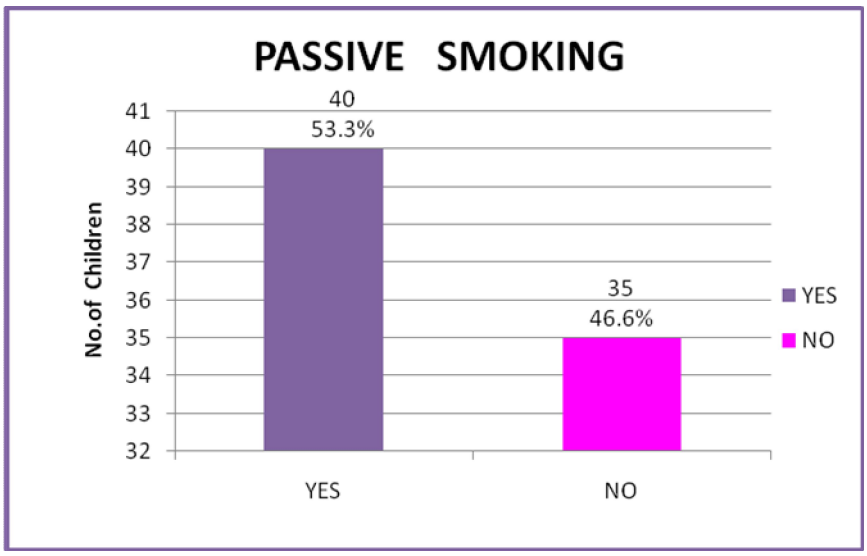
Table 4 Serum IgE levels based on family History

Family History	No. of cases	Percentage	Average IgE
Parent with asthma	27	36%	974
Grandparent with asthma	13	17%	612.3
Both Parent and Grandparent with asthma	5	7%	1142
NO family history of Asthma	30	40%	311

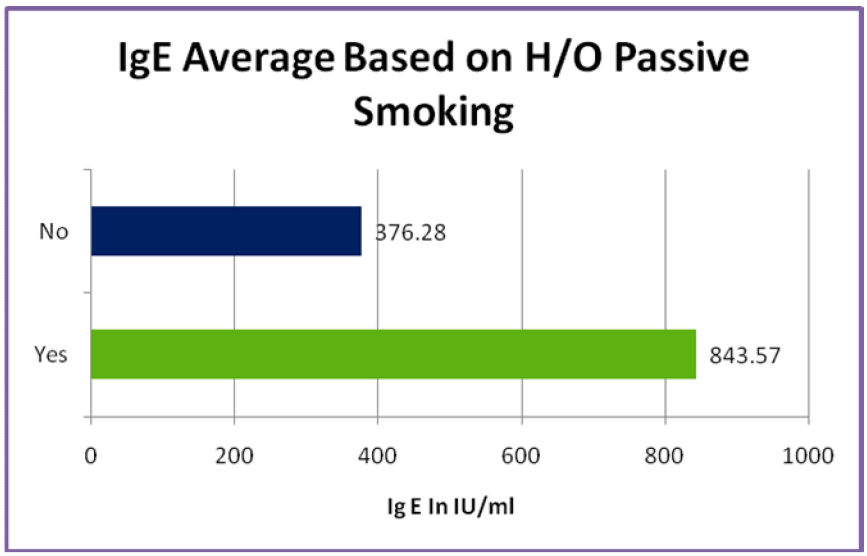
Serum IgE levels were higher in children with both Parents and Grandparents having asthma.


Family History
30
40%
27
36%
5
7%
13
17%
Parent withAsthma
Grant parent With Asthma
Parent and grant parent with Asthma
NO Family H/O of asthma

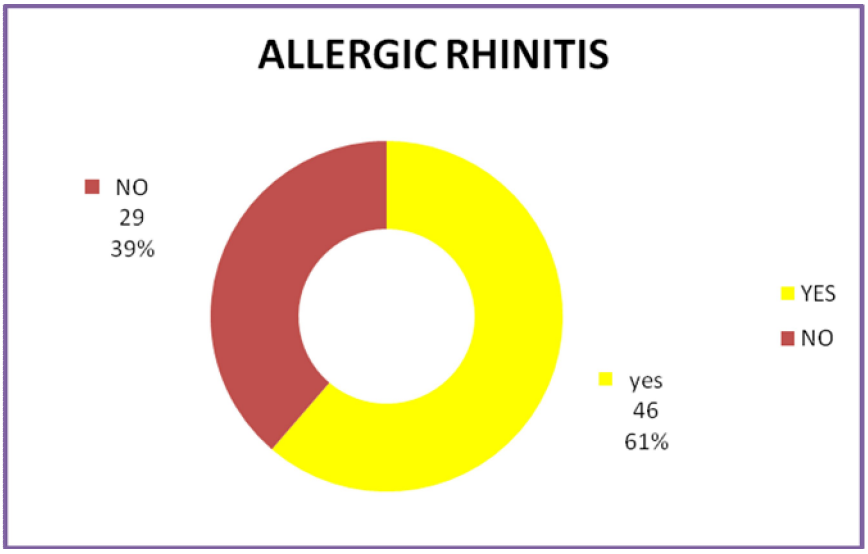

Ig E Average in Family History
NO Family H/O Asthma
Parent and G.Parent With asthma
Grandparent with asthma
Parent with asthma
311
1142
612.3
900.74
0
500
1000
1500
Parent with asthma
Grandparent with asthma
Parent and G.Parent With asthma
NO Family H/O Asthma



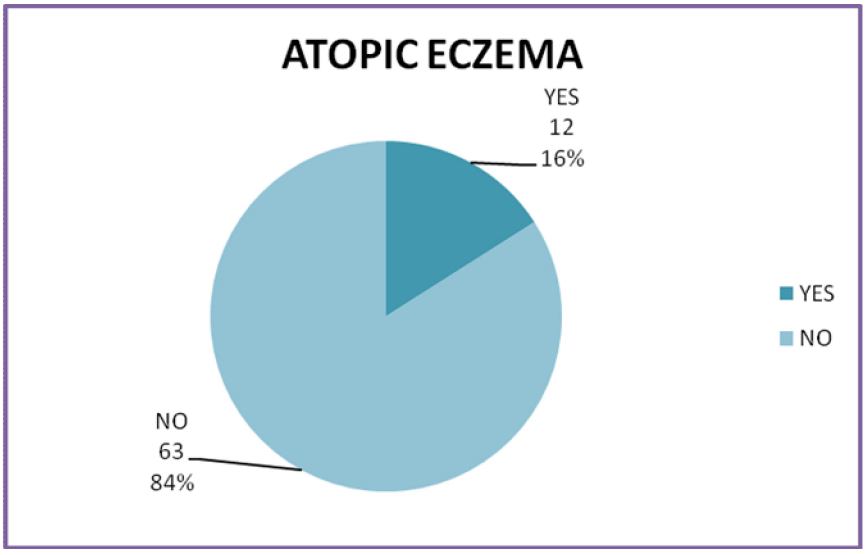
Majority of children had history of passive smoking.



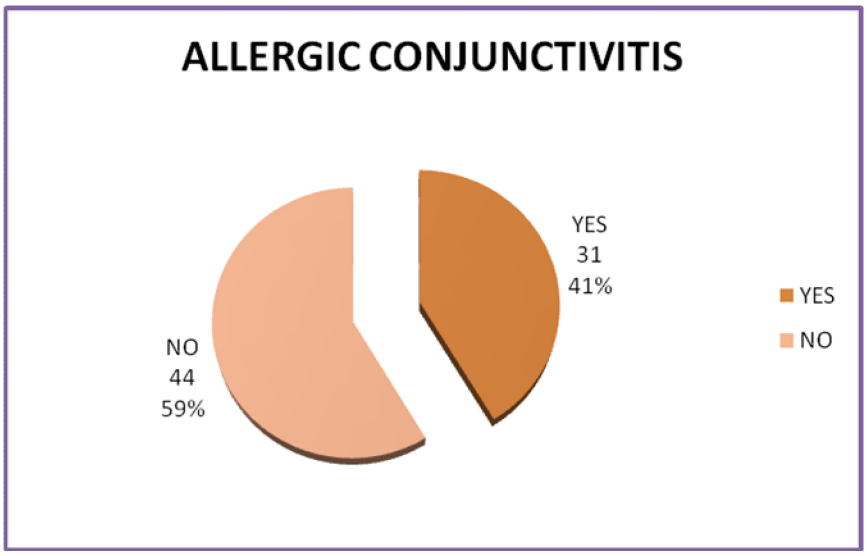
Children with history of passive smoking had higher IgE levels



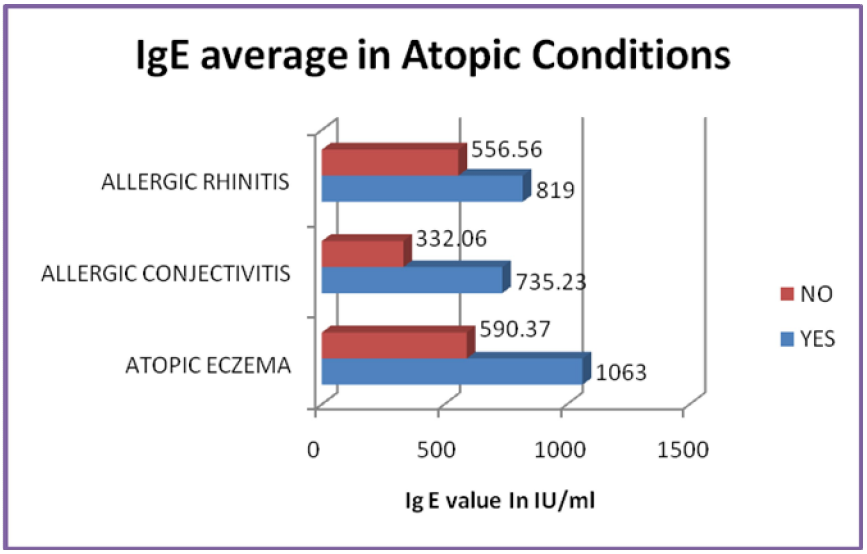
Majority of children (61%) had history of allergic rhinitis



Among the asthmatic children few cases (16%) had history of Allergic Eczema.



History of allergic conjunctivitis was present in some of the children (41%).

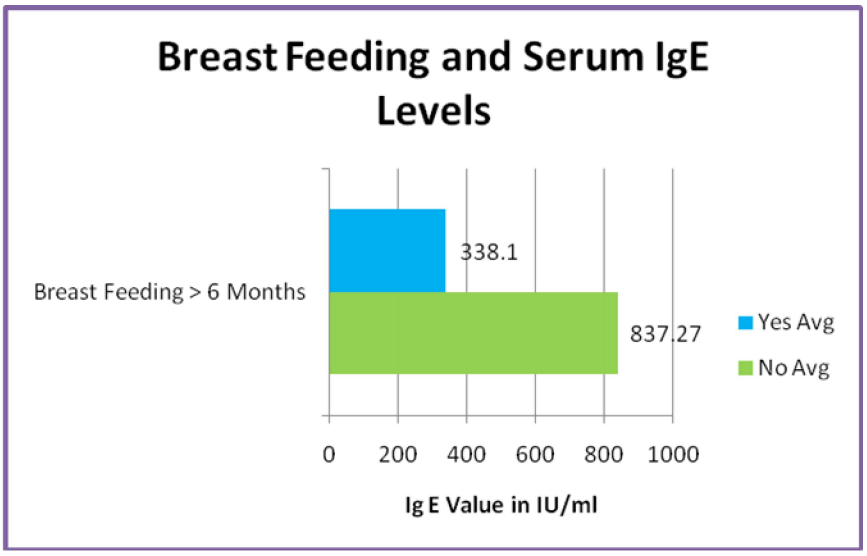


Children with Atopic eczema had maximum IgE Levels

Table 5 DURATION OF BREAST FEEDING

Duration of Breast feeding	No. Of Cases	Percentage
More Than 6 months	31	41.4%
Less Than 6 months	44	58.6%
Total	75	100%

Majority of Children were Breast fed for less than 6 months

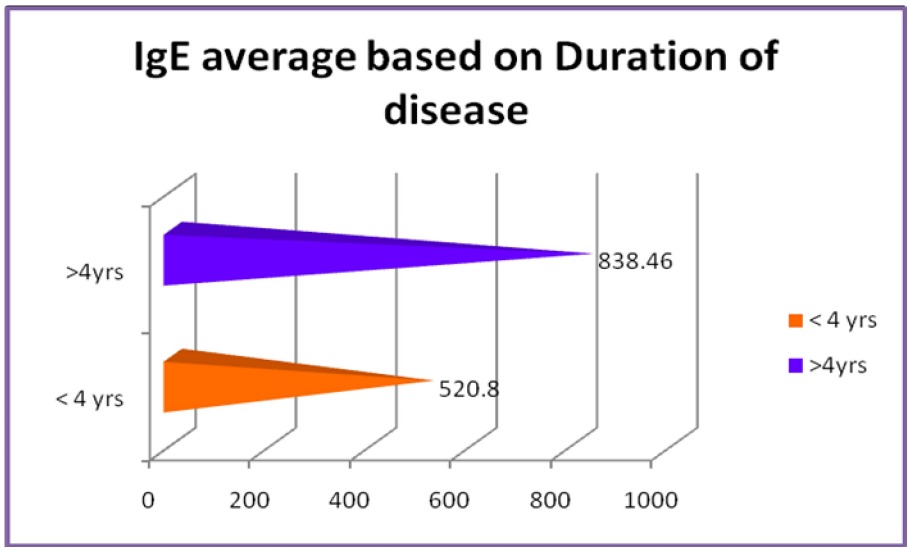


Children who were breastfed for more than 6 months had lower IgE levels compared to children who were breastfed for less than 6 months

Table 6 **Duration of the Disease**

Duration of Disease	No. of Cases	Percentage
Less than 4 years	49	65.34%
More than 4 Years	26	34.66%
Total	75	100%

Most of the children had duration of disease less than 4 years



Longer the duration of disease greater the IgE levels

Table 7 Association between Patient characteristics and Grading of Asthma

S.No	Variables(N=75)		n	%	p value	Inference
1	Duration of disease	<4 years	31	41	0.00	Significant association present
		>4 years	44	59		
2	Sex	Male	46	61	0.26	No Significant association
		Female	29	39		
3	Family History	1	27	36	0.00	Significant association present
		2	13	17		
		3	5	7		
		4	30	40		
4	H/o Passive smoking	1	42	56	0.00	Significant association present
		2	33	44		
5	Duration of breast feeding	1	31	41	0.00	Significant association present
		2	44	59		
6	Personal H/O Allergic conjunctivitis	1	21	28	0.37	No Significant association
		2	54	72		
7	Personal H/O Allergic rhinitis	1	11	15	0.00	Significant association present
		2	64	85		
8	Personal H/O Atopic eczema	1	46	61	0.00	Significant association present
		2	29	39		
	Analysis done through Epi Info 6 Version 3.3.2 Software					

Table 8 Association between IgE values and Clinical grading of Asthma

Clinical grading	n	Mean IgE value	Minimum IgE value	Maximum IgE value	p value*
INTERMITTENT	21	206.1905	70	640	0.00
MILD	16	501.25	465	830	
MODERATE	24	815.8333	795	1170	
SEVERE	14	1099.2857	1040	1220	
*Kruskal-Wallis H test for two groups (equivalent to Chi square)					
Inference :Mean value of IgE E is significantly associated with clinical grading of asthma					

DISCUSSION

DISCUSSION

Asthma is a chronic inflammatory disease of airways with increasing number of hospitalizations in young children worldwide. It poses a significant burden to the patient, family, health care systems and government. With advancement in management protocols and health education there has been a dramatic reduction in morbidity and mortality.

We studied 75 cases with symptoms and signs suggestive of asthma, who were attending the Outpatient as well as admitted in the Department of Pediatrics of Government Mohan Kumaramangalam Medical College Hospital, Salem from October 2011 to September 2012. Our observations are discussed below.

1. AGE DISTRIBUTION:

The proportion of cases in 5-8 years and 9-12 years were 49% and 51% respectively. In our study the prevalence of cases in both age groups were almost equal. According to Anupama et al the proportion of cases between 15 -30 years, 31 – 45 years and 46 -60 years were 28%, 47% and 25% respectively. In their study most of the cases were in 31 – 45 years of age.

2. SEX DISTRIBUTION :

Among 75 cases 46 were male children and 29 were female children, which corresponds to 61% and 39% respectively. This shows that boys are more affected than girls. But Anupama et al reported a female preponderance in asthmatic adults.

Male predominance in our study may be due to narrow airways and increased tone of airways in children which prompt them to increased airflow obstruction in response to various stimuli. Around puberty the prevalence becomes higher in female due to alterations in the thoracic size that occurs in male but not in female.

3. DISTRIBUTION ACCORDING TO SEVERITY:

Children were categorized into intermittent, mild, moderate and severe grades of asthma based on global initiative for asthma guides. The proportions of cases in different categories were 28%, 21%, 32% and 14% respectively. The prevalence of children with moderate asthma was found to be higher. Anupama et al showed that the proportion of cases was more in severe group of asthma.

4. AGE WISE DISTRIBUTION ACCORDING TO SEVERITY

In our study between 5-8 years the proportion of cases in Intermittent, mild, moderate and severe grades were 35%, 13%, 30% and 22% respectively. Majority of children in this age group were found to have intermittent asthma. In 9-12 years the proportions of cases in different categories were 21%, 29% 34% and 16% respectively. Most of the children in this age group belonged to moderate category.

Anupama et al reported that majority of cases between 15 – 30 years and 46 -60 years were in severe group and between 31 - 45 years belonged to moderate category.

5. SERUM IGE LEVELS BASED ON SEVERITY

In our study the mean IgE levels in controls and different grades of asthma were 89.90 IU/ml, 206.19 IU/ml, 501.25 IU/ml, 815.83 IU/ml and 1099.3 IU/ml correspondingly. Serum IgE levels were increased in all 4 categories of asthma patients when compared to normal control groups. As the severity of asthma increased, the serum IgE levels also significantly increased. Patients with severe bronchial asthma had higher IgE levels, than intermittent, mild and moderate grades. This finding was similar to earlier observations by Thirunavukarasu et al, Anupama et al and Hogarth et al.

The principal risk factor in the development of bronchial asthma is atopy. Atopy is production of increased amounts of IgE antibodies following exposure to various allergens.

There are several studies which explain the role of serum IgE in the development of chronic air flow obstruction. IgE plays an important role in airway obstruction by releasing number of inflammatory mediators like histamine, prostaglandins and leukotrienes.

The IgE receptors in atopic individuals send powerful signals which result in production of increased levels of Interleukin-4 from mast cells.

The elevated Interleukin-4 levels further result in over production of IgE antibodies. The reasons for elevated IgE levels in asthmatics may be due to increase in cellular elements of immune system as well as IgE dependent processes. It may also indicate some type of inbuilt propensity or presence of disease process relating to airway inflammation.

SERUM IGE LEVELS BASED ON AGE AND SEX

In our study IgE levels was found to be similar in both age groups and both sexes. Even though the proportions of cases were high in males, the serum IgE levels did not differ significantly in both sexes. Male preponderance in our study may be related to the airway anatomy than to serum IgE levels.

FAMILIAL PREDISPOSITION

In our study family history of asthma was present in 60% of the study population. 36% of children had either one of the parent with asthma, 13% of children had one of their grandparents with asthma and

around 7% of children had one of the parent as well as one of the grandparent with asthma.

There are numerous studies that have revealed that asthma has a strong genetic influence.In our study also we have found that there is a strong association between parent and grandparent status with the risk of development of asthma which is comparable to previous studies. Also the serum IgE levels in this study were higher in children who had parents and grandparents with asthma. This reflects that the severity was high in this group.

PASSIVE SMOKING:

In our study among 75 cases, 40 children had exposure to tobacco smoke. The severity of asthma and serum IgE levels was found to be higher in these children compared to those without a history of passive smoking. Passive smoking influences on the severity of asthma by increasing the bronchial responsiveness.

Number of studies has shown that children with history of passive smoking had greater bronchial responsiveness. Evans & Collaegues reported that the number of emergency room visits for asthma is more in

children if there is a smoker in the household. Our study also shows similar results that passive smoking has strong relationship to the severity of asthma.

PERSONAL HISTORY OF ATOPY:

In our study the Proportion of cases with history of allergic conjunctivitis, rhinitis and eczema were 41%, 61% and 16% respectively.

The severity was more in children with eczema who had elevated levels of serum IgE compared to allergic rhinitis and conjunctivitis. But Majority of children had history of allergic rhinitis. This was similar to the study by Mehmet et al.

There are animal studies that have identified an immune system activating protein called Thymic stromal lymphoprotein (TSLP) which played an important role in the association between atopic eczema and asthma.

It has been estimated that around 50-70% of children with atopic eczema subsequently develop asthma. In our study there is strong correlation between eczema and severity of asthma.

BREAST FEEDING :

In our study, 31(41.4%) cases were breastfed for more than 6 months and 44(58.6%) were breastfed for less than 6 months. Serum IgE levels were low in children who received breast feeding for more than 6 months. This reveals the protective role of breast feeding in the development of asthma.

Recent studies have also proved that breast feeding the child exclusively for 6 months could reduce the incidence of symptoms and severity of asthma to some extent.

DURATION OF THE DISEASE:

In our study number of children with duration of asthma < 4 years were 49 (65.34%) and duration > 4years were 26 (34.66%). Average IgE levels in children with duration of asthma less than 4 years was 520.8IU/ml and in children with duration more than 4 years it was 838.46 IU/ml. The severity was high in children who had symptoms for more than 4 years. According to Mehmet et al the duration of the disease did not correlate with the severity of asthma. But our results were comparable with the study of Anupama et al. This may be related to the progressive decline in lung function as the duration of Disease increases.

CONCLUSION

CONCLUSION

- Asthma continues to be a chronic disease which is increasing in prevalence among children worldwide. The morbidity and mortality due to asthma is still rising.
- Atopy, passive smoking, family history and duration of breast feeding remain the major risk factors in childhood asthma.
- There is strong correlation between atopy and severity of asthma. Especially severity is more in children with atopic eczema. Therefore early and effective management of Atopy could reduce the severity of asthma.
- Children with persistent exposure to passive smoking and with positive family history have severe asthma. These children should take necessary precautions to avoid the triggering factors that may contribute to morbidity.
- Exclusive and prolonged breast feeding plays a vital role in decreasing the severity of asthma.Insisting and promoting exclusive breast feeding for a period of 6 months and continuing it for long periods along with supplementary

feeds could significantly reduce the severity of asthma in children.

- Longer the duration of Asthma, the severity is more. Identifying the disease earlier and avoidance of triggering factors can reduce the frequent exacerbations.
- IgE has found to play a predominant role both in the prevalence and severity of asthma. Estimation of serum IgE levels and assessment of severity helps in effective management of asthmatic children.
- Based, on this study, Anti-IgE therapy will be beneficial as disease modifying agent in moderate to severe asthmatics. But further studies are needed to prove its effectiveness in children.
- There are numerous studies in Adults concerning asthma and serum IgE levels, but there are only very few studies in children. Our study will be valuable in the management of children with asthma and in reducing the morbidity and mortality.

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PROFORMA

PROFORMA

Name: Age: Sex:

Contact address:

Present complaints:

Breathing difficulty yes/no

Cough yes/no

History :

1. Age of onset of symptoms_____
2. Frequency of symptoms < 2 days/ wk > 2days/ wk

daily continuous

3. Nocturnal symptoms yes/no

If yes

No. of episodes in a month _____

4. Interference with physical activity / sleep yes/no
5. No. of exacerbations in a month _____
6. Febrile/ a febrile episode
7. Trigger induced attack yes/no

If yes Indoor/ Outdoor

8. Relief of wheeze with bronchodilators yes/no

9.Seasonal variation yes/no

10.Personal h/o Atopy yes/no

If yes

Eczema/ allergic conjunctivits/ allergic rhinitis/others

11. Family h/o asthma yes/ no

If yes parent/Grandparent/Both

12. Duration of Breast Feeding <6 months /> 6months

13. H/O Worm Infestation yes/No

General examination:

Ht: Wt:

Awake yes/no

Alert yes/no

Febrile/afebrile

Cyanosis yes/no

Investigations :

1) SpO2_____%

2)Serum IgE_____ IU/ml(Normal Male 0-230 IU/ml Female 0-170 IU/ml)

3)Peak Flow Metry: